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EXAMINER
SCHNIZER, RICHARD A

ART UNIT	PAPER NUMBER
1635	9

DATE MAILED: 06/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/839,574	Applicant(s) MANTHORPE ET AL.	
	Examiner Richard Schnizer	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,58,110 and 164-309* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☒ Claim(s) *194,196,198,200,219,221,223,225,288,290 and 292* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☒ Interview Summary (PTO-413) Paper No(s). 10 .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continuation of Disposition of Claims: Claims withdrawn from consideration are 165,167-174,185,188-190,201,203,207,208,211,227,233,234,236,237,246,248,252-254,258,261,267,279,282-284,294,296,300-302 and 304-307.

Continuation of Disposition of Claims: Claims rejected are 1,58,110,164,166,175-184,186,187,191-193,195,197,199,202,204-206,209,210,212-218,220,222,224,226,228-232,235,238-245,247,249-251,255-257,259,260,262-266,268-278,280,281,285-287,289,291,293,295,297-299,303,308 and 309.

DETAILED ACTION

An amendment was received and entered as Paper No. 8 on 3/22/02. Applicant's election of group II and of the species of sodium bicarbonate, influenza nucleoprotein, cationic lipids, Pluronic R 25R2, and intramuscular is acknowledged. It is noted that the election of Pluronic R 25R2 was made during a telephonic interview with Elizabeth Haanes on 6/4/02. Applicant's arguments regarding restriction of the invention into two groups are convincing, and group I is hereby rejoined. Applicant's arguments regarding the elections of species are unpersuasive. Applicant asserts that a search of surfactants would provide useful information regarding detergents polysaccharides, chelators, and DNase inhibitors. This is unpersuasive because it is unsupported by evidence, and because even if the required searches overlapped, they would not be coextensive. For example not all DNase inhibitors or chelators are surfactants. For these reasons the species election requirement is deemed proper and is made FINAL.

Applicant has identified at pages 2-4 of the response which claims are generic to, and which claims recite, each species. According to Applicant's lists, claims 1, 58, 110, 164, 166, 175-184, 187, 190-200, 202, 204-206, 209, 210, 212-226, 228-232, 235, 238-245, 247, 249-251, 255-256, 259-266, 268-278, 281, 284-293, 295, 297-299, 303, and 307-309 read on the elected species. The PTO finds a few exceptions to this list. First, claims 190 and 284 are not generic to the elected species because they do not read on or recite cationic liposomes. Second, claims 261 and 307 require administration by catheter therefore do not read on the elected species of intramuscular delivery. Third, the PTO finds that claims 186, 257, and 280 read on all the

elected species. Claims 186 and 280 recite viral polypeptides, a genus which includes the elected species of influenza nucleoprotein; and claim 257 recites the elected species of intramuscular delivery. For these reasons, claims 190, 261, 284, and 307 will not be among those considered in this Office Action, whereas claims 186, 257, and 280 will.

Claims 165, 167-174, 185, 188-190, 201, 203, 207, 208, 211, 227, 233, 234, 236, 237, 246, 248, 252-254, 258, 261, 267, 279, 282-284, 294, 296, 300-302, and 304-307 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected , there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Claims 1, 58, 110, 164, 166, 175-184, 186, 187, 191-200, 202, 204-206, 209, 210, 212-226, 228-232, 235, 238-245, 247, 249-251, 255-257, 259, 260, 262-266, 268-278, 280, 281, 285-293, 295, 297-299, 303, 308 and 309 and the species of sodium bicarbonate, influenza nucleoprotein, cationic lipids, Pluronic R 25R2, and intramuscular delivery are under consideration in this Office Action.

Claims limited to the species of auxiliary agent, Pluronic R 25R2, are found to be novel and unobvious over the prior art. In accordance with MPEP803.02, the Office has extended the search to a second species of auxiliary agent, *i.e.* Tween 80. Claims reciting this species have been found to be obvious over the prior art for the reasons given below.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 187, 235, and 281 are objected to under 37 CFR 1.75 as being substantial duplicates of claims 186, 234, and 280, respectively. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 187 differs from claim 186, claim 235 differs from claim 234, and claim 281 differs from claim 280, only in that claims 187, 235, and 281 substitute the term "immunogenic" for the term "antigenic" found in claims 186, 234, and 280. As noted below, under 35 USC 112, second paragraph rejections, these terms are synonyms, thus claims 186, 234, and 280 are drawn to precisely the same inventions as claims 186, 234, and 280, respectively.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 177-179, 184-189, 202, 215, 232-237, 247, 262-306, 308, and 309 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 177-179 are indefinite because it is unclear what is intended by "dissociation products" of "chloride ion". The specification fails to teach any dissociation products of chloride ion.

Claims 179 and 263-306, 308 and 309 are indefinite because it is unclear what is intended by "substantially free of chloride ion". The specification offers a non-limiting definition of this phrase at paragraph 83, page 31, i.e. the phrase "indicates that the amount of chloride ion added into the composition is insubstantial and that the addition cannot alter the transcription- and/or expression enhancing activity of the composition at a significant level." This definition is inadequate because it is not clear what is intended by "a significant level" of transcription or expression. Thus one of skill in the art cannot know the metes and bounds of the claims.

Claims 192-200, 217-225 are indefinite because they recite trademarks and trade names. See MPEP 2173.05(u), reproduced below for Applicant's convenience.

> **2173.05(u) Trademarks or Trade Names in a Claim**
>
> The presence of a trademark or trade name in a claim is not, per se, improper under 35 U.S.C. 112, second paragraph, but the claim should be carefully analyzed to determine how the mark or name is used in the claim. It is important to recognize that a trademark

> or trade name is used to identify a source of goods, and not the goods themselves. Thus a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. See definitions of trademark and trade name in MPEP § 608.01(v). A list of some trademarks is found in Appendix I.
>
> **If the trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of the 35 U.S.C. 112, second paragraph. Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. In fact, the value of a trademark would be lost to the extent that it became descriptive of a product, rather than used as an identification of a source or origin of a product. Thus, the use of a trademark or trade name in a claim to identify or describe a material or product would not only render a claim indefinite, but would also constitute an improper use of the trademark or trade name.**

Emphasis added. Because the recited trademarks are used as limitations to identify a particular material, the claims are indefinite. Examples of trademarks recited include Pluronic F68, Triton X-100, and Thesit. An example of a recited trade name is NONIDET NP-40.

The terms "enhanced" and "modulated" in claims 202, 247, and 295 are relative terms which render the claim indefinite. The terms "enhanced" and "modulated" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. These claims also recite "such an enhanced or modulated immune response" without antecedent basis.

Claims 215, 262, and 309 are indefinite because they require reducing the amount of a polynucleotide required to obtain a desired clinical response in a vertebrate, but it fail to provide any standard by which to determine whether or not a given amount constitutes a reduction. One of skill in the art is left to ask "reducing compared to what?" These claims also lack essential method steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Specifically, no step is recited in which the amount of polynucleotide is reduced, and as noted above, there is no step in which a comparison is performed which would allow one to determine what constitutes a reduced amount. These claims are also indefinite because the metes and bounds of "the amount of a polynucleotide required to obtain a desired clinical response in a vertebrate" are unclear. Different amounts of a given polynucleotide may give rise to more than one type of clinical response. Because the claim fails to correlate any specific amount of polynucleotide with any specific clinical response, one of skill in the art cannot know if an amount which gives rise to one response, but not to another response, infringes the claim or not. Furthermore, it is unclear what is intended by the phrase "clinical response". This phrase is not defined in the specification, and it is not clear how the term "clinical is meant to delimit the scope of the "response". Is any response a clinical response, so long as it occurs in a clinic?

Claims 184-189, 232-237, 278-283 are indefinite because the distinction between antigenic and immunogenic is unclear. These terms are recognized in the art as synonyms (see attached definition of "immunogenic" in Steadman's Medical Dictionary), yet they are recited as alternative limitations in the instant claims. Because the difference between the terms is not apparent, one of skill in the art cannot know what scope of protection Applicant seeks and the metes and bounds of the claims are unclear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 58, 110, 164, 166, 175, 176, 180-184, 186, 187, 191-193, 195, 197, 199, 202, 204-206, 209, 210, 212-218, 220, 222, 224, 226, 228-232, 235, 238-245, 247, 249-251, 255-257, 259, 260, and 262 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al (US Patent 6,120,794) in view of Ulmer, Science 259: 1745-1749 (1993), Wheeler et al (US Patent 5,861,397, Gregoriadis (FEBS LETT 402(3): 107-110, 199)) and Ishii et al (AIDS Res. Hum. Retrovir. 13(16): 1421-1428, 1997).

The claimed invention is a composition comprising 20-300 mM of a salt solution and 1 ng to 30 ng of a polynucleotide in aqueous solution encoding a polypeptide, and methods of delivering the composition to a vertebrate. Further embodiments of the invention require a transfection facilitating agent, an auxiliary agent, and stipulate a delivery route. Applicant has elected for examination an embodiment wherein the polypeptide is influenza nucleoprotein, the salt is sodium bicarbonate, the transfection facilitating agent is a cationic lipid, the auxiliary agent is Pluronic R 25R2, and the administration route is intramuscular.

Liu teaches nucleic acid compositions and methods for delivering them to vertebrate cells in vivo. See abstract. The composition may comprise e.g. an aqueous solution with 100 micrograms of DNA encoding a polypeptide. See column 10, lines 21-25; column 21, lines 30-38; and claim 1. The nucleic acid may also be mRNA. See column 9, lines 37-59, especially line 39. The composition may be buffered with bicarbonate. See column 8, lines 62-66. The composition comprises cationic lipids, including any cationic lipid which is effective for use in liposomes or for producing lipid complexes capable of delivering biologically active material to cells. See e.g. paragraph bridging columns 5 and 6. A colipid may be included, and the ratio of colipid to cationic lipid may be within the range of 2:1 to 1:2. See e.g. Table 1 at column 13. The composition may comprise the surfactant Tween 80. See column 7, lines 33 and 55; and Tables 1-4. Delivery may be intramuscular. See column 11, lines 24-32, especially line 27; and see claim 19. The composition may comprise a colipid, particularly DOPE. See column 7, lines 56-67, and Tables 1-4. Liu does not teach a nucleic acid encoding influenza nucleoprotein; the sodium salt of bicarbonate in a concentration of about 20-300 mM; or Pluronic R 25R2.

Ulmer teaches a method of inducing a protective immune response in a mouse by intramuscular injection of naked DNA comprising an expression cassette encoding influenza nucleoprotein. See entire document, especially abstract.

Wheeler teaches a compositions and methods for nucleic acid-mediated vaccination. The compositions may comprise 28 mM sodium bicarbonate. Wheeler teaches that the cationic liposomes DMRIE and GAP-DLRIE are useful for delivering nucleic acids to cells, and teaches a

composition comprising DLRIE and DOPE in a 1:1 molar ratio. See *e.g.* column 2, line 60 to column 3, line 3; column 7, lines 32-35; and column 14, lines 22-53.

Gregoriadis teaches that immunization by intramuscular injection of nucleic acids encoding antigens can be improved by us of cationic liposomes.

Ishii teaches that cationic liposomes are a strong adjuvant for DNA immunization.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the method and micellar complexes of Liu to deliver the influenza nucleoprotein expression vector of Ulmer. First, one would have been motivated to modify the method of Ulmer by using cationic liposomes as a delivery vehicle, because Gregoriadis and Ishii teach that the use of cationic liposomes constitutes an improvement over naked DNA delivery. Then one would have been motivated to substitute the method and micellar complexes of Liu for those of Gregoriadis or Ishii because Liu teaches that the disclosed micellar complexes are stable, whereas stability is a major problem limiting the use of liposomes. See column 1, lines 8-13, 32-36, and 49-51. Liu is silent as to which salt of bicarbonate is used in the method, and as to the concentration of bicarbonate. However, one of ordinary skill in the art seeking guidance as to which salt to use, and in what concentration, would have looked to Wheeler who teaches that the delivery of nucleic acid/cationic lipid compositions may be carried out in solutions comprising 28 mM bicarbonate (2.4 g Na bicarbonate/L). See column 13, lines 38-48.

It would have been obvious to use the cationic lipids DMRIE or GAP-DLRIE because Liu teaches that any cationic lipid which is effective for use in liposomes or for producing lipid

complexes capable of delivering biologically active material to cells may be used, and Wheeler teaches that these lipids are effective for this purpose. Furthermore, Wheeler teaches that DMRIE can be superior to DOTMA, a cationic lipid suggested for use by Liu.

Claim 110 is included in this rejection because the composition of Liu comprises little or no NaCl as evidenced by the fact that addition to 200 microliters of the composition of 6 microliters of 5M NaCl resulted in a solution of 150 mM NaCl. See column 21, lines 31-38.

Claims 175 and 176 are included in this rejection because, although none of the cited references teaches sodium bicarbonate in a concentration of 100-200 mM, generally differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating that this concentration is critical. See MPEP 2144.05(b). In this case, the concentrations in question are clearly not critical for the practice of the invention because the specification teaches that a broader concentration will function. This is reflected in claim 1 which recites a range of 20-300 mM sodium bicarbonate. The cited art is combined to teach the general conditions of the claims, i.e. a composition comprising 28 mM sodium bicarbonate. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Claims 215 and 262 are included in the rejection because the cited art teaches both the composition and the required method step, i.e. administration of the claimed composition to a vertebrate.

Thus the invention as a whole was *prima facie* obvious.

Claims 240 and 242 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu, Ulmer, Wheeler, Gregoriadis, and Ishii as applied to claims 1, 58, 110, 164, 166, 175, 176, 180-184, 186, 187, 191-193, 195, 197, 199, 202, 204-206, 209, 210, 212-218, 220, 222, 224, 226, 228-232, 235, 238-245, 247, 249-251, 255-257, 259, 260, and 262 above and further in view of Wheeler (WO 00/57917, published 10/5/00).

Liu, Ulmer, Wheeler, Gregoriadis, and Ishii can be combined to render obvious a method of delivering to a cell in vivo a composition comprising a 1 ng to 30 mg of a polynucleotide encoding influenza nucleoprotein in aqueous solution, 20-300 mM sodium bicarbonate, the surfactant Tween 80, and cationic lipids. These references do not teach the cationic lipid GAP-DMORIE, or the colipids DpyPE and DMPE.

Wheeler WO 00/57917 ('917) teaches compositions and methods for polynulceotide-based vaccination and immune response. In particular '917" teaches the use of GAP-DMORIE combined with a colipid, such as DOPE, DPyPE or DMPE. See abstract, and page 4, lines 3-11 and 19-24. "917' also shows that administration of plasmid DNA with DMORIE, or with DMORIE and DPyPE combined, leads to an enhanced immune response against influenza nucleoprotein relative to that obtained using naked DNA. See page 30, lines 1-3; page 31, lines 1-3; and page 33, lines 11-16.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use GAP-DMORIE as a cationic lipid in the method of Liu, Ulmer, Wheeler, Gregoriadis, and Ishii. One would have been motivated to do so because Liu teaches that any cationic lipid which is effective for use in liposomes or for producing lipid complexes capable of delivering biologically active material to cells may be used, and '917' teaches that these lipids are effective. Furthermore,'917' teaches that GAP-DMORIE and the combination of GAP-DMORIE and colipid DPyPE is superior to naked DNA. One would have been motivated to use DMPE as a colipid because '917' indicates that when using GAP-DMORIE one should use a colipid such as DMPE.

Thus the invention as a whole was *prima facie* obvious.

Claims 177-179, 263-266, 268-278, 280, 281, 285-287, 289, 291, 293, 295, 297-299, 303, 308, and 309 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu, Ulmer, Wheeler, Gregoriadis, and Ishii as applied to claims 1, 58, 110, 164, 166, 175, 176, 180-184, 186, 187, 191-193, 195, 197, 199, 202, 204-206, 209, 210, 212-218, 220, 222, 224, 226, 228-232, 235, 238-245, 247, 249-251, 255-257, 259, 260, and 262 above and further in view of Hartikka et al (Gene therapy 7(14): 1171-1182, 7/2000), and Wheeler (WO 00/57917, published 10/5/00)..

Liu, Ulmer, Wheeler, Gregoriadis, and Ishii can be combined to render obvious a method of delivering to a vertebrate cell *in vivo* a composition comprising a 1 ng to 30 mg of a polynucleotide encoding influenza nucleoprotein in aqueous solution, 20-300 mM sodium

bicarbonate, the surfactant Tween 80, and cationic lipids. These references do not teach a method of delivering a polynucleotide to a vertebrate in which the chloride ion concentration of the aqueous solution is less than about 125 mM. Rather, for the purpose of intramuscular delivery, Liu teaches the use of 150 mM NaCl.

Hartikka teaches a method of expressing influenza nucleoprotein *in vivo* by intramuscular injection of plasmid DNA. Hartikka teaches that expression can be improved if 150 mM sodium phosphate is substituted for the 150-154 mM sodium chloride which is frequently used by those of skill in the art. See abstract.

Wheeler WO 00/57917 ('917) teaches compositions and methods for polynulceotide-based vaccination and immune response. In particular '917" teaches the use of GAP-DMORIE combined with a colipid, such as DOPE, DPyPE, or DMPE. See abstract, and page 4, lines 3-11 and 19-24. '917' also shows that administration of plasmid DNA with DMORIE, or with DMORIE and DPyPE combined, leads to an enhanced immune response against influenza nucleoprotein relative to that obtained using naked DNA. See page 30, lines 1-3; page 31, lines 1-3; and page 33, lines 11-16.

The '917' reference is intended to be applied to claims 268 and 270 for the purpose of rendering obvious the species of GAP-DMORIE, and GAP-DMORIE combined with a colipid, such as DPyPE or DMPE.

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the 150 mM sodium phosphate of Hartikka for the 150 mM sodium chloride of Liu.

One would have been motivated to do so in order to improve the amount of polypeptide expression obtained in the method, as taught by Hartikka.

It would have been obvious to one of ordinary skill in the art at the time of the invention to further modify the invention through the use of GAP-DMORIE as a cationic lipid. One would have been motivated to do so because Liu teaches that any cationic lipid which is effective for use in liposomes or for producing lipid complexes capable of delivering biologically active material to cells may be used, and '917' teaches that these lipids are effective. Furthermore, '917' teaches that GAP-DMORIE and the combination of GAP-DMORIE and colipid DPyPE is superior to naked DNA. One would have been motivated to use DMPE as a colipid because '917' indicates that when using GAP-DMORIE one should use a colipid such as DMPE.

Thus the invention as a whole was *prima facie* obvious.

Conclusion

No claim is allowed.

Claims 194, 196, 198, 200, 219, 221, 223, 225, 288, 290, and 292 are objected to as being dependent on a rejected base claim, and because they are not limited to the scope of the elected invention. These claims would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, and if limited to the elected species of sodium bicarbonate, influenza nucleoprotein, cationic lipids, Pluronic R 25R2, and intramuscular delivery.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Leguyader, can be reached at 703-308-0447. The FAX numbers for art unit 1632 are 703-308-4242, and 703-305-3014. Additionally correspondence can be transmitted to the following RIGHTFAX numbers: 703-872-9306 for correspondence before final rejection, and 703-872-9307 for correspondence after final rejection.

Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 703-305-3413.

Richard Schnizer, Ph.D.

JAMES KETTER
PRIMARY EXAMINER